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Legal Division - Patent Department

To: USPTO

Fax No.: 571-273-8300

Date: March 22, 2006

Re: Serial No. 10/785,326 (Docket X-11057C)

From: Gilbert T. Voy

Phone: 317-276-2966

No. Pages 10

Enclosures:

1. Brief for Appellants
2. Fee Sheet

PAGE 1/10 * RCVD AT 3/22/2006 4:33:01 PM [Eastern Standard Time] * SVR:USPTO-EFXRF-5/21 * DNIS:2738300 * CSID:317 276 3861 * DURATION (mm-ss):02-32

Please type a plus sign (+) inside this box → +

FEE TRANSMITTAL

Effective December 8, 2004

Complete if Known	
Serial No.	10/785326
Application Date	February 24, 2004
US Nat'l Entry Date (if applicable)	
First Named Inventor	COHEN Fredric Jay
Group Art Unit	1614
Examiner Name	DELACROIX MUIRHE, CYBILLE
Conf. No.	9685
Attorney Docket Number	X11057C

TOTAL AMOUNT OF PAYMENT	($) 500.00

METHOD OF PAYMENT (check one)

1. [X] The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:

Deposit Account Number: 05-0840
Deposit Account Name: Eli Lilly and Company

[X] Charge Any Additional Fee Required
[ ] Charge the Issue Fee set in 37 CFR 1.18 at the time of allowance

FEE CALCULATION

1. **In connection with the filing, search and exam fees**

Code	Description	Fee	Fee Paid
1011	Basic filing fee (Utility)	$300.00	
1111	Utility search fee	$500.00	
1311	Utility examination fee	$200.00	
	SUBTOTAL (1)	($)	

Code	Total claims	Extra	Fee Paid ($)
1202	___ - 20 =	___ X 50 =	$

Independent claims

1201	___ - 3 =	___ X 200 =	$

1203	Multiple Dependent Claim	Yes or No	360 = (if yes)	$

Claims and Excess Length Fees

1081 Total length (spec + drawings)
___ - 100 = ___ excess pages
$_____

No extra charge for first 100 pages. Must pay $250 for each adtl 50 pages (or fraction thereof).

SUBTOTAL (2) ($)

FEE CALCULATION (continued)

3. **ADDITIONAL FEES**

Large Entity Fee Code	Large Entity Fee ($)	Fee Description	Fee Paid
1051	130	Surcharge-late filing fee or oath	
1052	50	Surcharge-late provisional filing fee or cover sheet.	
1053	130	Non-English specification	
1251	120	Extension for reply within first month	
1252	450	Extension for reply within second month	
1253	1,020	Extension for reply within third month	
1254	1,590	Extension for reply within fourth month	
1255	2,160	Extension for reply within fifth month	
1401	500	Notice of Appeal	
1402	500	Filing a brief in support of an appeal	$500.00
1452	500	Petition to revive-unavoidable	
1453	1,500	Petition to revive-unintentional	
1502	1,400	Utility issue fee (or reissue)	
122	130	Petitions to the Commissioner	
1801	790	Request for Continued Examination (RCE)	

Other fee (specify)

Other fee (specify)

Other fee (specify)

Other fee (specify)

SUBTOTAL (3) ($)500.00

SUBMITTED BY		Complete (if applicable)	
Typed or Printed Name	Gilbert T. Voy	Reg. Number	43,972
Signature	Gil Voy	Date	3/22/06

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office on the date shown below.

Linda Durbin
Type or print name of person signing certification
571-273-8300

Linda M. Durbin March 22, 2006
Signature Date

PATENT APPLICATION
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Before the Board of Patent Appeals and Interferences

First Appellant	:	Cohen, *et al.*	
Serial Number	:	10/785,326	
Filed	:	February 24, 2004	Group Art Unit: 1614
For	:	METHODS OF PREVENTING BREAST CANCER	Examiner: Delacroix Muirhei
Docket No.	:	X-11057C	

BRIEF FOR APPELLANTS, Cohen, et al.

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Appellants appeal the Final Rejection dated July 28, 2005 (and Advisory Action dated February 24, 2006) of claims 147, 148, 151 and 152 of this application.

Real Party in Interest

Eli Lilly and Company is the real party in interest in the instant appeal, as the inventors of the above-referenced application assigned the present invention to Eli Lilly and Company on February 24, 1998, March 12, 1998 and January 23, 2006.

Related Appeals and Interferences

There are no related appeals or interferences.

Status of Claims

Claims 19 and 145-152 are currently pending in the instant application. Claims 19, 145, 146, 149 and 150 have been allowed. Claims 147, 148, 151 and 152 stand finally rejected under 35 U.S.C. §112, 1st paragraph for allegedly lacking an enabling disclosure.

Status of Amendments

Claims 19 and 145-152 stand as amended by Appellants reply of January 23, 2006.

Summary of Invention

The instant invention, as embodied in the disputed claims, relate to a method for reducing the likelihood of incurring or developing estrogen-dependent breast cancer, wherein said incurrence or development of breast cancer is in the first instance, in a post-menopausal woman diagnosed as being in need of such therapy which comprises administering orally to said woman a once-daily dose of a pharmaceutical composition wherein said composition comprises about 60 mg of raloxifene hydrochloride.

Issues

Is the presently articulated rejection of claims 147, 148, 151 and 152 proper in view of the enablement requirement of 35 U.S.C. §112, 1st paragraph?

Grouping of Claims

Claims 147, 148, 151 and 152 stand or fall together.

Case for Appellants

I. Procedural History

In the Office Action of October 1, 2004, the Examiner rejected claims 147, 148, 151 and 152 as allegedly lacking an enabling disclosure. In arriving at this conclusion, the Examiner recited and performed an "In re Wands" analysis of those claims. For brevity, Appellants will only highlight those Wands factors upon which there is a disagreement. Specifically, the Examiner made the following disputed findings:

> **(2) The state of the prior art**
> *[C]omplete* "prevention" [or breast cancer] has yet to be recognized. ... (emphasis added to "[C]omplete"; see also use of term "complete" prevention found in the Examiner's analysis of the 7th and 8th Wands factor)
>
> **(4) The predictability or unpredictability of the art**
> [T]he lack of significant guidance from the present specification or prior art with regard to the actual prevention of breast cancer in a human, with the claimed compound as the active ingredient makes practicing the claimed method unpredictable. ...
>
> **(6) The amount of direction or guidance presented**
> The claims require the" primary prevention" of breast cancer in postmenopausal women, that is to say, a method of thwarting or warding of breast cancer in post-menopausal women. However, Applicant's specification provides no guidance to enable one of ordinary skill in the art to practice the claimed method. Instead there appears to be guidance on reducing the likelihood of breast cancer in post-menopausal women who are at risk for breast cancer, i.e. a woman with a personal history of breast cancer (a breast cancer survivor) or a post-menopausal woman who has a family history of the disease (please see page 11, lines 5-12, page 20 etc).
>
> Moreover, the specification does not provide guidance as to how one of ordinary skill in the art would accomplish the objective of preventing breast cancer in a postmenopausal woman or how a post-menopausal woman could be kept from even being susceptible to cancer. Nor is there any guidance provided as to a specific protocol to be utilized in order to show the efficacy of the presently claimed active agent for primary prevention of breast cancer.

> **(8) The quantity of experimentation necessary**
> Since (1) the current therapeutic approach in the art is to the treatment and not the prevention of breast cancer and (2) the specification lacks guidance or working examples demonstrating the primary prevention of breast cancer in a post-menopausal woman, one of ordinary skill in the art would be burdened with undue experimentation to completely prevent or ward off breast cancer in any post-menopausal woman.
>
> Additionally, it is highly unlikely, and the Office would require experimental evidence to support the contention, that the claimed active agent, raloxifene, could actually prevent breast cancer, by simply orally administering an amount of the claimed active agent. The specification fails to enable one of ordinary skill in the art to practice the prevention of cancer.
>
> Finally, the term "prevention" is synonymous with the term "curing" and both circumscribe methods of absolute success. Since absolute success is not reasonably possible with most diseases/disorders, especially those having etiologies and pathophysiological manifestations as complex/poorly understood as breast cancer, the specification, which lacks an objective showing that breast cancer can actually be prevented or cured, is viewed as lacking an adequate written description of the same.

In their response of January 23, 2006, Appellants amended the claims in dispute by replacing the term "de novo" with the term "in the first instance." In the Advisory Action of February 24, 2006, the Examiner maintained this rejection of the disputed claims stating, "Such an amendment is a rewording of the claims, for upon reference to the specification page 6, lines 30-31, it is clear that "in the first instance" is another way of describing "primary prevention".

II. Argument: Appellants Claims are Enabled

As a preliminary matter, Appellants respectfully reassert that the claims at issue are NOT directed to the "cure" or "prevention", complete or otherwise, of breast cancer. Appellants respectfully assert that such constructions ignore the supporting specification, in particular the description of the "TEST PROCEDURE" found on pages 20-26, and more importantly the language of the rejected claims themselves and the language of the claim upon which all of the rejected claims depend.

As stated in their after final response of January 23, 2006,

> [The] rejected claims all depend from claim 145. Claim 145 recites:
>
> A method for **reducing the likelihood of incurring or developing estrogen-dependent breast cancer** in a post-menopausal woman diagnosed as being in need of such therapy comprising ....
>
> Thus, all of the pending claims, including the rejected claims are directed to **reducing the likelihood of incurring or developing** breast cancer. None of the claims are directed to "prevention" of breast cancer in the sense that the United States Patent and Trademark Office has recently been interpreting this term. ...
>
> Claim 147 and the other claims rejected for an alleged lack of enablement are directed to reducing the likelihood of incurring or developing estrogen-dependent breast cancer *in the first instance*.

Emphasis in the original.

Moreover, Appellants respectfully assert that reducing the likelihood (risk) of incurring or developing estrogen-dependent breast cancer in the first instance, as called for in the rejected claims, is fully enabled, described and established within their application as filed. Appellants respectfully direct the Board's attention to the description of a clinical trial (TEST PROCEDURE) beginning at page 20 of their specification wherein the ability of raloxifene HCl to lower the relative risk of developing or incurring breast cancer, in a study initially designed to determine the efficacy of raloxifene HCl to prevent or treat osteoporosis in postmenopausal women, is specifically examined and demonstrated. Excerpts (beginning at page 20, line 22) from this description are reproduced below:

> Patients were randomly assigned to receive either placebo, 30 mg, 60 mg, 120 mg or 150 mg of [raloxifene hydrochloride] per day, orally. All patients and investigators are blinded to study drug assignment (double-blind design). ...

Subjects selected for these studies are postmenopausal women (at least 2 years from the time of the last menstrual period), ages range from approximately forty-five to eighty years.

Typical exclusion criteria from participation in these studies included: .... **Most important of the exclusion criteria was the exclusion of women with present or past personal history of breast cancer or other estrogen-dependent neoplasia**. These exclusion criteria generate a population of subjects which reflects the general population in regard to the risk of developing breast carcinoma, or in other words, those persons at no particular increased risk of developing breast cancer. ...

All potential patients were required either to have a baseline mammogram or ultrasound evaluation of the breast, or to have had one of these procedures in the 12-month period preceding study entry. In most studies, a two-year follow-up mammogram is required; however, annual mammograms are recommended. ...

In these placebo-controlled studies, the data clearly indicate that patients randomly assigned to raloxifene have a decreased incidence of breast cancer compared with patients randomly assigned to placebo. The estimate of crude relative risk for all patients diagnosed at least one month after random assignment to study drug is 0.36, with a 95% confidence interval (0.20, 0.64), **indicating a 64% decrease in the rate of breast cancer.** When the large treatment study is considered alone, the estimate of crude relative risk is 0.29, with 95% confidence interval (0.15, 0.55), **indicating a 71% decrease in the rate of breast cancer**. These results are highly statistically significant.

Because cancers diagnosed at least 1 year after randomization are most likely to represent cancers that were not clinically pre-existing, we have also analyzed the data considering only cases which occurred at least 12 months after randomization to study drug. For all placebo-controlled studies combined, the crude relative risk estimate is 0.23, with a 95% confidence interval (0.11, 0.45), **corresponding to a 77% decrease in the incidence of breast cancer.** For the large treatment study, the estimate of crude relative risk is 0.14, with a 95% confidence interval (0.06, 0.32), **corresponding to a 86% decrease in the incidence of breast carcinoma.**

Appellants assert that since the patients taking part in the study described above did not have a "present or past personal history of breast cancer," said clinical study demonstrated that, in fact, patients receiving raloxifene were at a reduced risk, relative to their counterparts receiving placebo, of developing or incurring breast cancer in the first instance. Thus, Appellants respectfully assert the findings that:

a) the claims are directed to complete "prevention" or curing of breast cancer;

b) that the specification does not provide significant guidance or a specific protocol for practicing the claimed invention;

c) that the ability of raloxifene HCl to actually reduce the risk of incurring or developing breast cancer is "unpredictable"; and

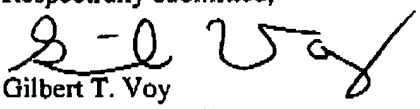
d) that the specification only provides guidance on reducing the likelihood of breast cancer in post-menopausal women who are at risk for breast cancer;

are clearly in error.

Summary

Appellants respectfully request that the Board reverse the Examiner's rejection of Claims 147, 148, 151 and 152. Such action by the Board is earnestly solicited.

Respectfully submitted,



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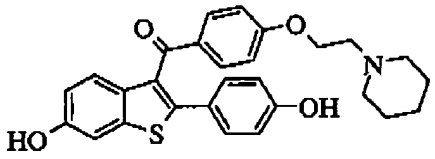
Eli Lilly and Company
Patent Division/GTV
Lilly Corporate Center
Indianapolis, Indiana 46285

March 22, 2006

Appendix: Pending Claims

19. The method of Claim 145 wherein said composition is administered to said woman for at least six months.

145. A method for reducing the likelihood of incurring or developing estrogen-dependent breast cancer in a post-menopausal woman diagnosed as being in need of such therapy which comprises administering orally to said woman a once-daily dose of a pharmaceutical composition wherein said composition comprises about 60 mg of the hydrochloride salt of a compound of the formula



146. The method of claim 145 wherein said composition is administered to said woman chronically.

147. The method of claim 145 wherein said incurrence or development of breast cancer is in the first instance.

148. The method of claim 146 wherein said incurrence or development of breast cancer is in the first instance.

149. The method of claim 145 wherein said woman is at increased risk of incurring or developing breast cancer.

150. The method of claim 146 wherein said woman is at increased risk of incurring or developing breast cancer.

151. The method of claim 147 wherein said woman is at increased risk of incurring or developing breast cancer.

152. The method of claim 148 wherein said woman is at increased risk of incurring or developing breast cancer.